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EXAMINER

KALLIS, RUSSELL

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RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte LARA MADISON, GJALT W. HUISMAN
and OLIVER P. PEOPLES

Appeal 2008-0228
Application 09/235,875
Technology Center 1600

Oral Hearing Held: April 17, 2008

Before TONI R. SCHEINER, LORA M. GREEN, and RICHARD M.
LEBOVITZ, *Administrative Patent Judges*.

ON BEHALF OF THE APPELLANT:

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PROCEEDINGS

MS. BEAN: Calendar Number 52, Mrs. Pabst.

JUDGE SCHEINER: Thank you. Good morning.

MS. PABST: Why don't you sit. Good morning.

JUDGE SCHEINER: Would you like to introduce your colleagues --

MS. PABST: Yes.

JUDGE SCHEINER: -- for the record, please.

MS. PABST: Thank you. I'm Patrea Pabst. This is Michael Oliver Peoples from Metabolix, who is the Assignee and been in on a lot of these, and this is my brand-new patent agent, Carolyn Burn --

JUDGE SCHEINER: Welcome.

MS. PABST: -- who is here to learn. We appreciate the opportunity to be here.

JUDGE SCHEINER: Um-hum.

MS. PABST: This is one of those cases where rarely do I think that we need an Oral Hearing as much as this because there are so many pages that I think you wear out just trying to read it.

The real issue here, as I understand it, is whether or not the prior art Fukui anticipates inherently or make obvious the claimed subject matter. And I'm actually going to turn this over in a second to Dr. Peoples because I'm sure you have questions. But what we've done is try to put together a diagram, and if I can hand copies. This summarizes in picture form the arguments and evidence that is of record, and I think makes it a little easier to say in one minute what we've spent a few years trying to say in words.

So, if you look at this little diagram, what we have at the bottom on the left is what we claim. We claim a genetically engineered organism that has been engineered to express thiolase, reductase, PHA polymerase so that

it can go from butanol or butyrate to produce a very specific polymer; polyhydroxybutyrate-hydroxyhexanoate, PHBH.

The prior art which is shown at the top is an organism described in Fukui that expresses enzymes that allow that organism to produce the same polymer from a different substrate, a C6 substrate.

JUDGE GREEN: Just one question. This is -- I think it comes down to the Examiner is saying wherein the bacteria can utilize butanol or butyrate to mean that's just merely intended use.

MS. PABST: Okay, but it's not. If I, if I could just finish for a second because I'm going to address exactly that point, because you are absolutely right, it's a major issue. If you look at Schubert, which is another piece of prior art cited. This has the same starting organism as Fukui, the *Alcaligenes*, and it has the thiolase and the reductase. And if you feed it butanol or butyrate, it produces a different polymer, 3HB.

So, what we have here is an organism that has been engineered to express an effective amount, which is in the claims, of these enzymes that allow it to go from a substrate butanol or butyrate to an end product, PHBH, because enzymes, as you know -- and this is my whole -- this is in answer to your question. It's not intended use. You have to have the enzymes with the requisite substrate specificity in an effective amount so that when you provide it with a substrate -- and you all know enzymes probably better than I do -- it takes through that process, converts the starting material to the next intermediate which is converted to the next intermediate to produce the product that is claimed.

So, we have here a claim to an organism that has been genetically engineered to express enzymes effective amount having requisite substrates specificity in amount that does this. Bacteria express a lot of enzymes and they have different substrate specificity. If you look at the polymerase in this field, the first -- and I, and I started with Dr. Peoples on this patent when he was at MIT back in 1986, a long time ago.

And, my first introduction to this enzyme, and it was a PHB polymerase, and then we came along and there was something called a PHA polymerase, and he said wait a minute, what happened here.

Well, depending on the source of that polymerase, they had different substrate specificities, and so they're not the same enzyme. One acts on shorter carbon substrates than the other and they come from different sources. SO, to get to the desired end product from a desired starting material you have to select both the enzymes with the necessary substrates specificity.

You go from the substrate you want to feed it, which in this case is a very cost-effective substrate, to produce the desired product.

Now, what I'm going to do is ask Dr. Peoples to answer anymore of your questions just because I'm sure you have some. But again, that's what's in the claims here. That's why it's different, and we think that the evidence summarizes -- the little page here shows those differences.

JUDGE LEBOVITZ: Well, first of all, I hope this is not new evidence.

MS. PABST: It's not new evidence because it's not evidence. This is simply -- if you read our Reply Brief, this is exactly what is said in the Reply

Brief. All we did was give you a picture of it. It is nothing new. There's nothing new. It's, it's the same information that's there. I'm just trying to cut down on the words because it was easier to point to this.

JUDGE LEBOVITZ: Well, I don't -- what I was going to say was I don't find it helpful because the claim has genes in there and I think what -- at least what I'm trying to understand now is whether those genes with those function are in the cited prior art. I understand about the relationship between genes and pathways, but --

MS. PABST: Well --

JUDGE LEBOVITZ: -- what we're trying to dissect here is whether the bacteria that's cited has those genes.

MS. PABST: Okay.

JUDGE LEBOVITZ: That's first step.

MS. PABST: Okay. Well let me respond just briefly to that point. The first is that the Examiner has done something that I find rather unusual here in that because he cited a reference, Fukui, that he had to admit didn't disclose our claimed subject matter, he cited probably eight or ten additional references to try to say, well apparently discloses these features.

The bottom line was he didn't cite a piece of prior art that goes from our starting material to our end product. The prior art, Fukui, goes from a completely, totally different substrate that is acted on and must be acted on by enzymes that have a different substrate specificity because they are long carbon chain substrates. They are C6 substrates, not short chain butanol or butyrate substrates.

And you all know enzymes, they have a specificity that says that the substrate determines whether they will be acted upon and what they are converting to. So, Fukui does not disclose the same enzymes. What Fukui discloses works perfectly well to get to the same end product, but he has to go from the substrate he discloses and has to have different enzymes because he starts with a different substrate.

Now, Schubert starts with the same starting material with the same bacteria, alkyliginease, and comes up with a different end product. If you look at all the art cited, there is no question that each of these genes is disclosed somewhere. They were all known genes.

JUDGE SCHEINER: Is it your position that the gene may or may not be in there, but it's not there in a sufficient amount?

MS. PABST: Well, there, there are two parts to this, and, and Dr. Peoples can respond to it better, but I think it's quite clear. Our claim recites certain essential genes. If these genes encoding these enzymes are not present and they're not present in an effective amount --

JUDGE SCHEINER: That was my question.

MS. PABST: Yeah, you will not get this product from this substrate.

JUDGE LEBOVITZ: Well, where's the evidence that, for example, 3-ketothiolase that convert say butyryl-CoA and acetyl-CoA to 3-ketohexanoyl? Where's the evidence? This is a simple question, that that gene is not present in the cited reference and/or not present in an amount that it would be capable of the activity recited in the claim. You may have it. I'm just asking if you can put that to the record --

MS. PABST: Well, Schubert --

JUDGE LEBOVITZ: -- where. Excuse me.

MS. PABST: Schubert starts with butyrate and uses an *Alcaligenes*. He doesn't produce the same product.

JUDGE LEBOVITZ: I understand that. I was just asking a question about --

MS. PABST: Okay, that's the evidence.

JUDGE LEBOVITZ: I was asking a question about limitation in the claim.

MS. PABST: The limitation in the claim -- now, I'm going to comment on one thing, and this is one of the realities that we all have to deal with at the Patent Office these days, is that we go through a lot of Examiners. And I'm sure you saw from looking at this case, that we had multiple Examiners and that we had discussions with the Examiner. The language in the claim as currently proposed was language he proposed. It was not language that we proposed. We had different language. We amended the claim to use his language, and then he came back and said, that's not what I had in mind, and we're here on Appeal.

We can only -- we, we try in some ways to accommodate the Patent Office and what they request. The bottom line here, and this is what is important, is we were trying to take and define an organism that is in commercial use. It's a very commercially important organism that has been developed by Metabolix to go from this cheap substrate to a very valuable polymer.

When they started this process, they spent several years developing this organism because it wasn't out there. So, could somebody have

screened thousands and thousands and thousands of organisms and perhaps have found something that would get to this? I can't say there's no possibility of it, but the company wouldn't have spent years and millions of dollars getting there if they could have picked up Fukui or Schubert and just used what they had. It just wouldn't have worked that way.

So, I, I think the question of inherency is an interesting question, and I think you have to look at the case law on inherency, and it quite clearly says the mere possibility that something could occur is not sufficient for inherency. I can't say there's no organism out there, but we don't know of any. And, the company found that it was cheaper and faster and easier to spend millions of dollars and years to develop this organism than to screen all possible candidates that were out there.

So, I think on an inherency point, I have a problem with the rejection because, first, a mere possibility is not sufficient, and I think the fact that the Examiner had to cite so many additional references to try to make an inherency argument says that, at best, it's a mere possibility and the evidence indicates it probably isn't that case.

And, then you have to look at obviousness. Was there a recognition in the art that you would want to go from butanol or butyrate to this specific polymer? And I don't think that this art makes that leap. That's pretty much where we are.

JUDGE SCHEINER: There were several other rejections, weren't there?

MS. PABST: There were some new rejections raised in the Examiner's answer, which I think we effectively dealt with --

JUDGE SCHEINER: That's right.

MS. PABST: -- in, in our Reply Brief, for example.

JUDGE SCHEINER: There were new grounds.

MS. PABST: You know, it said well you didn't provide the gene sequence for these enzymes that are Independent Claims. Well, what we had done of course is provide citations. These are known enzymes. There are no novel enzymes that we claiming. These were all known organisms. They had to be selected for substrate specificity. They had to be engineered into the organism, and the levels of expression had to be engineered, and then the system had to be optimized to ultimately come up with the product. Of course, it was ultimately optimized for the commercial embodiment that's out there.

This is a very important polymer in the, the industry at this point.

JUDGE SCHEINER: Okay. Do you have anything further?

JUDGE LEBOVITZ: No.

JUDGE SCHEINER: Do you have anything further? We're okay if you -- unless you have something further.

MS. PABST: No. You know, I have great respect for this Panel and that you all understand this technology, so I appreciate the opportunity to be in front of you.

JUDGE SCHEINER: Okay. Well, thank you for coming in.

MS. PABST: Thank you.

COURT REPORTER: One quick question. The spelling of -- the correct spelling of Schubert and Fukui, please.

MS. PABST: Oh.

COURT REPORTER: Okay.

MS. PABST: There's Fukui --

JUDGE LEBOVITZ: F U K U I.

MS. PABST: There's Schubert.

COURT REPORTER: Okay, thank you.

JUDGE LEBOVITZ: S C H U B E R T.

JUDGE GREEN: It's easier just to hand it to him.

COURT REPORTER: Thank you so much.

JUDGE SCHEINER: Thank you, appreciate it.

JUDGE LEBOVITZ: Thank you.

JUDGE SCHEINER: Thank you.

(Whereupon, the proceedings concluded at 10:37 a.m. on
April 17, 2008.)